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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/734,548	12/12/2003	Shyam S. Mohapatra	USF-T187XC1	4609

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EXAMINER	
SHIN, DANA H	
ART UNIT	PAPER NUMBER
1635	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/21/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/734,548	MOHAPATRA ET AL.	
	Examiner	Art Unit	
	Dana Shin	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 21-27* is/are pending in the application.

4a) Of the above claim(s) *4-6 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,7-11,13 and 21-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11-8-04, 2-27-07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of claims 21-27 pertinent to siRNA in the reply filed on February 27, 2007 and November 7, 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Status of Claims

Claims 4-6 and 12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant has cancelled claims 14-20 and added 23-27. Accordingly, claims 1-13 and 21-27 are pending, and claims 1-3, 7-11, 13, and 21-27 are currently under examination on the merits.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-

filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/319,780, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. The disclosure of 60/319,780 does not contain the instantly claimed subject matter, "siRNA" or "interfering RNA", nor does it adequately describe a method performed *in vivo* in a patient. Accordingly, claims 1-3, 7-11, 13, and 21-27 are denied an earlier priority date. Applicant is encouraged to point out the particulars in support of siRNA or interfering RNA in response to this Office action. In this absence of such evidence, the instant filing date, December 12, 2003 will stand as the earliest filing date for claims 1-3, 7-11, 13, and 21-27.

Specification

The disclosure is objected to because of the following informalities:

The abstract of the instant application contains the term, "thereof". Applicant is reminded of the proper language and format for an abstract of the disclosure. The form and legal phraseology often used in patent claims such as "thereof" should be avoided.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The claims are drawn to a method of inhibiting an RSV infection in a patient comprising administering an siRNA that decreases endogenous PKC activity.

Nowhere in the instant disclosure does appear the term "interfering RNA" or "siRNA". Therefore, the instantly claimed subject matter was not described in such a way as to reasonably convey to one skilled in the art that the inventors had possession of the claimed invention at the time the application was filed.

Claims 1-3, 7-11, 13, and 21-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to a method of inhibiting an RSV infection in a patient comprising administering PKC inhibitor, wherein the PKC inhibitor is an siRNA molecule.

As broadly claimed without reciting any specific structure of the claimed PKC inhibitor, the generic claims, claims 1 and 3, embrace any PKC inhibitors (e.g., siRNA, antisense oligonucleotide, antibody, peptide, ribozyme, chemical compound, etc). Further, claims 21-27 do not recite any specific structure of the claimed interfering RNA (e.g., SEQ ID NO), which effectively inhibits an RSV infection in a patient as claimed in the instant case.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and /or chemical properties, functional characteristics, structure/function correlation, or any combination thereof.

Although the specification discloses a chemical compound RO318220 and PKC-α/β pseudosubstrate peptide as a potential candidate for inhibiting an RSV infection in a patient based exclusively on *in vitro* cell transfection data, these exemplified PKC inhibitors are not representative of the structurally defined genus recited in the claims. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath, Inc. v. Mahurkar, 935 F.2d at 1563, 19 USPQ2d at 1116 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (see page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (see page 1116).

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of making it. The compound itself is required. See *Fiers v. Revel*, 984 F.2d 1164, 1168, 25 USPQ2d 1601,1604-05 (Fed. Cir. 1993).

Corollary to the instant claims to broad genera of inhibitors and siRNAs, in *Fiddes,* claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class since the specification provided only the bovine sequence (See *Fiddes v. Baird,* 30 USPQ2nd 1481 at 1483).

Claims 1-3, 7-11, 13, and 21-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is an enablement rejection.

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'." (Wands, 8 USPQ2d 1404). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of

one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The claims embrace only *in vivo* methods.

The instant specification is silent about siRNA-mediated gene therapy in a patient having an RSV infection, and further, the disclosure on "Gene Therapy" (Example 6) is entirely prophetic without any working embodiments. Even a couple of species of PKC inhibitors disclosed in the specification are not tested for their ability to inhibit an RSV infection in a living human patient *in vivo*.

The DNA-mediated therapeutics, especially siRNA technology, were not fully enabled even after the instant application was originally filed as the Patil et al. reference teaches. See citation. It explicitly teaches that "Despite many favorable characteristics and signs of possible clinical victories (see Table 1), the introduction of DNA-based drugs for human use can be best described as limited, with rare successes." See page E62. To corroborate this statement, it was reported that the pharmaceutical anti-PKC alpha antisense compound (known as Affinitak) failed to show therapeutic efficacy in humans when evaluated in patients with advanced non-small cell lung caner. Applicant's attention is directed to Table 1 on page E62 and the Biotech Week citation (Atlanta: April 9, 2003, page 74), which supports that the siRNA therapeutics would require undue experimentation before they can be used *in vivo* in humans.

The state of the art of making and using siRNAs to modulate gene expression, given the nucleotide sequence of a target gene, was such that one skilled in the art could readily design, make, and use siRNAs that would reduce the expression of the gene, at the time of filing.

Nonetheless, this facile design and use of siRNAs are applicable only to a method drawn to *in vitro* gene inhibition performed on a benchtop or in a cell culture room. The siRNA technology at the time of filing was relatively nascent, and further, *in vivo* therapeutic applications of the siRNA technology were far from being well-established. That is, one skilled in the art could not have readily extrapolated any *in vitro* data obtained from the benchtop experimental science to predict the requisite *in vivo* pharmaceutical/therapeutic effects in a living organism/host. In fact, the state of the "gene therapy" art was far from being both well-understood and widely practiced at the time of filing.

In order to overcome the art-recognized unpredictability of siRNAs as therapeutic agents, the specification must provide sufficient guidelines so as to produce the claimed therapeutic effects when the instantly claimed methods are practiced by one of ordinary skill in the art. As stated above, the specification is completely silent about the instantly claimed siRNA that can inhibit an RSV infection in a human patient suffering from the RSV infection or not suffering from the infection.

The working examples provided by the applicant do not support any *in vivo* effects of inhibiting an RSV infection in a living organism. Moreover, the instant disclosure does not set forth any specific guidance/direction as to how to practice the instantly claimed treatment method (i.e, method steps or protocols) or how to obtain the therapeutic effects required by the claims.

As stated above, neither the state of the art of using siRNA gene therapy nor the content of the disclosure provides guidelines to practice the claimed therapeutic method without undue experimentation. Conception is not achieved until reduction to practice has occurred, regardless

of the complexity or simplicity of the method of treating a patient comprising administering a PKC inhibitor that is an siRNA molecule. For an actual reduction to practice, the invention must have been sufficiently tested to demonstrate that it will work for its intended purpose, but it need not be in a commercially satisfactory stage of development. See, for example, *Scott v. Finney*, 34 F.3d 1058, 1062, 32 USPQ2d 1115, 1118-19 (Fed. Cir. 1994).

Further, claims embrace any and all genera of siRNA molecules that decease, not targeted to, PKC in a patient (human or non-human) who is or is not suffering from an RSV infection. As such, the scope of the claims is so broad that one of ordinary skill in the art would not have been able to carry out the steps to required to practice the full scope of the claims. Corollary to the instant case, in *In re Wright*, 999 F.2d 1557, 27 USPQ2d 1510 (Fed. Cir. 1993), the court affirmed the Board's decision and stated that the evidence did not show that a skilled artisan would have been able to carry out the steps required to practice the full scope of claims which encompass "any and all live, non-pathogenic vaccines, and process for making such vaccines, which elicit immunoprotective activity in any animal toward any RNA virus." 999 F.2d at 1562, 27 USPQ2d at 1513 (original emphasis).

In view of all the factors and the totality of the teachings that the activity of DNA-based drugs are unpredictable *in vivo*, undue experimentation would be required of a person of ordinary skill in the art to practice the instantly claimed invention, thus claims 1-3, 7-11, 13, and 21-27 are not enabled.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dana Shin whose telephone number is 571-272-8008. The examiner can normally be reached on Monday through Friday, from 8am-4:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin
Examiner
Art Unit 1635

JANE ZARA, PH.D.
PRIMARY EXAMINER